

Notice of Allowability

Application No.

10/625,059

Applicant(s)

WILDE ET AL.

Examiner

Art Unit

Eric S. Olson

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Applicant's communication submitted April 19, 2007.
2. ☒ The allowed claim(s) is/are 1-3,7 and 9-19.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

SHAOJIA ANNA JIANG, PH.D.
SUPERVISORY PATENT EXAMINER

Detailed Action

This office action is a response to applicant's communication submitted April 19, 2007, wherein claims 1, 7, 9, 16, and 19 are amended and claims 4-6 and 8 are cancelled. This application claims benefit of provisional application 60/398334, filed July 24, 2004.

Claims 1-3, 7, and 9-19 are pending in this application.

Claims 1-3, 7, and 9-19 as amended are examined on the merits herein.

Applicant's amendment, submitted April 19, 2007, with respect to the rejection of instant claims 1-6 and 9-19 under 35 USC 112, second paragraph, for being indefinite for failing to clearly and distinctly define substituents in the recited structures, has been fully considered and found to be persuasive to remove the rejection as the claims as amended now clearly and distinctly define the identity of the substituents. Therefore the rejection is withdrawn.

Applicant's amendment, submitted April 19, 2007, with respect to the rejection of instant claims 1-6 and 9-19 under 35 USC 112, first paragraph, for lacking enablement for a method comprising administering any compound in formula I, has been fully considered and found to be persuasive to remove the rejection as the claims as amended involve only species of a narrower formula that is fully enabled by the specification. Therefore the rejection is withdrawn.

Applicant's amendment, submitted April 19, 2007, with respect to the rejection of instant claims 1-16 and 19 under 35 USC 112, first paragraph, for lacking enablement for a method of treating any cancer whatsoever, has been fully considered and found to be persuasive to remove the rejection as the claims as amended are drawn only to treatment of those specific cancers involving a p53 nonsense mutation. Therefore the rejection is withdrawn.

Applicant's amendment, submitted April 19, 2007, with respect to the rejection of instant claims 1-18 under 35 USC 112, first paragraph, for lacking enablement for a method of preventing cancer, has been fully considered and found to be persuasive to remove the rejection as the claims as amended are drawn only to treatment of cancer. Therefore the rejection is withdrawn.

Applicant's amendment, submitted April 19, 2007, with respect to the rejection of instant claims 1-3, 6, 9-11, and 18-19 under 35 USC 103(a), for being obvious over Sanghvi et al., has been fully considered and found to be persuasive to remove the rejection as the claims as amended are drawn only to therapeutic methods involving monocyclic compounds that are patentably distinct from those disclosed by Sanghvi et al. Therefore the rejection is withdrawn.

Applicant's arguments, submitted April 19, 2007, with respect to the rejection of instant claims 1-19 under 35 USC 103(a), for being obvious over Kaddurah-Daouk et

al., has been fully considered and found to be persuasive to remove the rejection as Kaddurah-Daouk et al. is not seen to provide enabling disclosure for the supposed antitumor properties of clitocine, as discussed below under reasons for allowance. Therefore the rejection is withdrawn.

Reasons for Allowance

Currently, claims 1-3, 7, and 9-19 are pending in this application and have been examined on the merits herein. The claimed compounds and pharmaceutical compositions described in the instant claims are not seen to be taught or fairly suggested by the prior art.

Reasons for allowance are as follows: The claimed therapeutic methods are seen to be novel and non-obvious over the prior art and are directed to subject matter that is adequately described and enabled by Applicant's specification. For example, the examples on pp. 83-88 demonstrate that clitocine, a compound of the claimed invention, is capable of promoting read-through of premature stop codons, restoring full-length gene expression, and exerting a cytotoxic activity on tumor cells carrying a p53 nonsense mutation. This disclosure is sufficient to enable one skilled in the art to make and use the invention for compounds of the structure recited in instant claim 1, as these compounds bear a close structural similarity to clitocine. Furthermore, the examples on pp. 69-82 enable one skilled in the art to make these and similar compounds, and one skilled in the art could easily test them for nonsense read-through activity as described in the aforementioned examples. As regards the scope of cancers treatable by this

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method, the range of cancers included within the claimed invention, such as those recited in claims 11 and 13-15, all share the common mechanism of a p53 nonsense mutation. Although they arise in different tissues, they are all expected to be treatable by restoring expression of the full-length p53 gene product. As describe in Zambetti et al., (Reference included with PTO-1449) it is well known in the art that mutations in the p53 gene, such as nonsense mutations, are oncogenic and produce a cancerous phenotype in the cells they occur in. These mutations are common across many different types of cancer, as described in p. 2, lines 16-29 of the instant specification. P. 53, line 19 – p. 55, line 4 of the instant specification discloses that restoring full-length wild-type p53 expression is reasonably expected to cause apoptosis in cancer cells bearing a nonsense mutation in the p53 gene. It is expected that a method of suppressing these nonsense mutations would be useful for treating a cancer that contains a nonsense mutation in p53. In addition, one skilled in the art is capable of routinely measuring full-length p53 expression in biopsy samples to determine whether a patient's tumor contains a mutated p53 gene. This biopsy test is a routine part of the current state of the art in oncology, and would not require any particularly burdensome or unpredictable experimentation to determine which patients are candidates for treatment, as described on p. 55, line 19 – p. 56, line 4 of the instant specification.

The claimed therapeutic method is not known in the prior art. Although clitocine is known in the art, for example in the reference Moss et al. (included with PTO-1449) it is not known to promote read-through of nonsense mutations or to be useful for treating cancers with nonsense mutations in the p53 gene. The specific cell line L1210 that was

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tested in Moss et al. is not a cell line bearing a p53 nonsense mutation, and is thus outside of the scope of the instant claims. While Kaddurah-Daouk et al. includes clitocine in a list of compounds potentially useful for treating viral tumors having elevated levels of purine metabolic enzymes, this reference does not provide a reasonable expectation of success in practicing the claimed invention using clitocine as an anticancer agent. In particular, the only therapeutic agents tested by Kaddurak-Daouk et al. are creatine kinase inhibitors having no structural similarity to clitocine, and of the various creatine kinase inhibitors tested, only 4 of 14 were found to be active as antitumor agents, indicating a high level of unpredictability in the subject matter. Note that the claims of Kaddurah-Daouk et al. are not drawn to clitocine, or to any compositions or methods involving clitocine.

While the claimed invention is not patentably distinct from that of claims 1-9 and 18-31 of copending application 11/048659, the '659 application has not been allowed. Therefore the double patenting rejection over this reference is withdrawn as it is the sole remaining rejection.

For these reasons, the subject matter is allowable over the prior art.

Accordingly, Applicant's amendment submitted April 19, 2007 is sufficient to remove all rejections made in the prior office action as discussed above and to place the application in condition for allowance.

Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled, "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Eric Olson

A handwritten signature in black ink, appearing to read "Eric Olson", with a long vertical line extending upwards from the end of the signature.

Patent Examiner

AU 1623

6/14/07

Anna Jiang

A handwritten signature in black ink, appearing to read "Anna Jiang", followed by the date "6/15/07".

Supervisory Patent Examiner

AU 1623